PHARMACARE NEWSLETTER

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This newsletter provides information on the PharmaCare program for British Columbia's community pharmacists. Please circulate among dispensing staff.

PharmaCare on the Web:
www.healthservices.gov.bc.ca/pharme

VIOXX® Withdrawn from Market Worldwide

On September 30, 2004, Merck &. Co., Inc. voluntarily withdrew Vioxx® (rofecoxib), its arthritis and acute pain medication, from the worldwide market due to safety concerns.

Merck & Co, Inc. stated that it withdrew Vioxx® when three-year data from a clinical trial (designed to evaluate the efficacy of the drug in preventing the recurrence of colorectal polyps) showed an increased relative risk for cardiovascular events, such as heart attack and stroke, after 18 months of treatment with Vioxx®. Merck reported that results for the first 18 months of the trial did not show an increased risk of these events.

As of September 30, 2004, Merck had informed the regulatory authorities in countries where the drug was marketed of its decision and had begun notifying health care practitioners.

As of that date, PharmaCare Special Authorities for Vioxx®, which had been a limited coverage drug under PharmaCare, were no longer issued and existing Special Authorities for the drug were terminated. PharmaCare encourages patients to contact their physician to discuss appropriate alternative treatments.

For inventory questions, pharmacies should contact the manufacturer directly.

Patients and health care professionals may obtain information from Merck Frosst (the Canadian affiliate of Merck & Co., Inc.) by visiting www.merckfrosst.com or calling the Merck Frosst Customer Information Centre at 1-800-567-2594.

Background

The Therapeutics Initiative (TI), established in 1994 by the Department of Pharmacology and Therapeutics in cooperation with the Department of Family Practice at the University of British Columbia, provides physicians and pharmacists with up-to-date, evidence-based, practical information on rational drug therapy. The TI is an independent organization, which is at arms length from the government, the pharmaceutical industry and other vested interest groups.

The TI acts in an advisory capacity to PharmaCare with respect to clinical drug reviews.

In its Therapeutics Letter (Issue 39, January/February 2001), the TI review of the clinical evidence at that time concluded that patients on rofecoxib had less complicated and symptomatic ulcers but more myocardial infarctions than patients on naproxen.

In a later Therapeutics Letter (Issue 43, November/December 2001), the TI concluded that, based on FDA data from the CLASS and VIGOR studies, COX-2 selective inhibitors were associated with an increased incidence of serious adverse events as compared to non-selective NSAIDs.

PharmaCare originally listed rofecoxib available only under exceptional circumstances through PharmaCare's Special Authority process subject to stringent criteria.

Inclusion of Clozapine in the Low Cost Alternative (LCA) Program

Effective **November 25, 2004**, clozapine will be included as an eligible benefit for Plans B, C, F, I and G, under PharmaCare's Low Cost Alternative (LCA) Program.

Please note that the inclusion of clozapine in the LCA Program will not affect patients already receiving full benefit coverage of Clozaril® 25 mg and 100 mg. These patients will continue to receive full benefit coverage of this drug under indefinite PharmaCare Special Authorities that will be in effect on PharmaNet on November 25, 2004. No action is required by physicians or pharmacists to secure continuing full benefit coverage of Clozaril® for these patients (subject to the usual rules of the patient's PharmaCare plan).

Claims for all first-time prescriptions for clozapine dispensed on or after November 25, 2004, will be reimbursed as follows:

Chemical Name	DIN	MAN	Brand Name	LCA Status	Price
Clozapine 25mg	894737	NVR	Clozaril Tab 25mg	P	0.6844
	2248034	APX	Apo-Clozapine Tab 25mg	F	
	2247243	GPM	Gen-Clozapine Tab 25mg	F	
Clozapine 100mg	894745	NVR	Clozaril Tab 100mg	P	2.7448
	2248035	APX	Apo-Clozapine Tab 100mg	F	
	2247244	GPM	Gen-Clozapine Tab 100mg	F	

Health Canada Advisory for Health Professionals - Clozapine

Monitoring of patients taking clozapine in Canada

Please note that, in June 2004, Health Canada posted an advisory regarding the monitoring of patients being treated with clozapine. For your convenience, Health Canada's Advisory for Health Professionals is included in this newsletter.

Health Canada / Santé Canada — Health Products and Food Branch / Direction générale des produits de santé et des aliments

The Health Products and Food Branch (HPFB) posts on the Health Canada web site safety alerts, public health advisories, press releases and other notices as a service to health professionals, consumers and other interested parties. These advisories may be prepared with information in the HPFB database, including pre-market and post-market files, as well as market authorization holders and other stakeholders. Although the HPFB grants market authorizations or licences for therapeutic products, we do not endorse either the product or the company. Any questions regarding product information should be discussed with your health professional.

June 22, 2004

Subject: Monitoring of patients taking clozapine in Canada

Dear Health Care Professional:

The Marketed Health Products Directorate (MHPD) and the Therapeutic Products Directorate (TPD) would like to draw your attention to important upcoming revisions to the Product Monographs of all clozapine products marketed in Canada. These revisions will strengthen the labelling and address ongoing issues around patient consent for the sharing of information between registries. As you know, monitoring of patients with the use of registries is the risk mitigation strategy in place to address the known risk of agranulocytosis.

Revisions to clozapine Product Monographs will emphasize the following:

1. the switching of a patient from one brand of clozapine to another must not be done by a pharmacist unless he/she obtains a new, registry-specific patient registration form filled out by the prescribing physician.
2. the physician has to inform his/her patient about the potential sharing of information between clozapine registries and document if there is consent from the patient to allow it, in order to ensure the safe use and continuous monitoring of patients taking clozapine.
3. the responsibility of physicians concerning the sending of the mandatory laboratory results (white blood cell counts and differential) to the appropriate registry will be limited to informing the laboratory where the patient's haematological results have to be sent.
4. weekly monitoring of neutrophils and white cell counts for four weeks at the end of the treatment is necessary only in case of cessation of all clozapine treatment.

Due to a significant risk of agranulocytosis, patients on clozapine and their treating physicians and dispensing pharmacists have to be enrolled in registries, which are currently specific to each market authorization holder. Patients must undergo regular haematological tests to

monitor their total white blood cell and absolute neutrophil counts. Between 1991 and 2003, clozapine was distributed by a single manufacturer, and patients were monitored by that manufacturer's specific registry. The introduction of generic clozapine in the last year has led to the establishment of other registries.

After consultations with representatives from market authorization holders, the Canadian Psychiatric Association (CPA), the Schizophrenia Society of Canada and the National Association of Pharmacy Regulatory Authorities (NAPRA), Health Canada is taking the following steps to ensure the safe use and continuous monitoring of patients taking clozapine in Canada:

- inclusion of a statement in the registry-specific Patient Registration Form signed by the treating physician (see proposed text in attachment #1) certifying that the patient has been informed of the necessary sharing of information between clozapine registries to enable continuous monitoring and safe use of the medication. The inclusion of this text in the Patient Registration Forms is necessary to overcome ongoing problems with the exchange of information between registries, caused in part by some potential implications of the Personal Information Protection and Electronic Documents Act (PIPEDA), the federal legislation protecting personal information in the private sector, including health information. As a preventive measure and to avoid any confusion, physicians may also ask patients already on clozapine to fill out the updated Patient Registration Form.

- A "Questions and Answers" patient information leaflet, prepared in collaboration with the Schizophrenia Society of Canada, is also provided (see attachment #2) to help physicians to document the actual consent from the patient on information exchange between registries.

- Appropriate revision of clozapine Product Monographs to reflect the above.

Any questions related to a clozapine product or a registry should be directed to the company concerned. Any further questions on clozapine Product Monographs updates should be adressed to the Therapeutic Products Directorate (TPD) by phone: (613) 957-0368, by fax: (613) 952-7756 or by email: TPD-general-DPT-Generale@hc-sc.gc.ca. Any further questions related to this letter should be adressed to the Marketed Health Products Directorate (MHPD) (613) 946-5140, by fax: (613) 946-6011 or by email: mhpd_dpsc@hc-sc.gc.ca.

The implementation of these steps will permit the achievement of a more efficient network of independent registries, and therefore improve the continuity of care of patients treated with clozapine.

We thank you in advance for your collaboration in the implementation of these changes.

original signed by

Christopher Turner, MD FRCPC
Director General
Marketed Health Products Directorate

original signed by

Robert Peterson, MD, MPH, PhD
Director General
Therapeutic Products Directorate

Attachment #1

STATEMENT BY TREATING PHYSICIAN
[Note: Statement proposed to be included in Patient Registration Form]

I, the treating physician, will ensure that blood testing, date blood cell count and differential for this patient identified below as required by the clozapine Product Monograph is performed at the specified frequency. I understand that no pharmacy will dispense any brand of clozapine to my patient without my prior knowledge and permission regarding which brand is being dispensed. In this way, I will be able to inform the laboratory to send my patient's results to the appropriate manufacturer's clozapine database. I will not prescribe clozapine until the non-rechallengeable status of this patient has been verified.

I have informed the patient and he/she has not objected to the release of relevant safety information held within a clozapine database to any other clozapine database of an approved manufacturer of clozapine in Canada if needed for the safe utilization of this medication and/or for the continuous monitoring of the patient. The information which may be released includes the non-rechallengeable haematological status of the patient, date blood cell counts and absolute neutrophils counts, dates and other information as may be relevant to the safe treatment of the patient with clozapine.

Name of treating physician:

Physician license number:

Signature of treating physician:

Date: (DD/MM/YYYY) / /

Patient Initials:

Date of Birth (DD/MM/YYYY): / /

Gender: M ☐ F ☐

Province / Health Card Number: /

Attachment #2

Q & As Regarding Patient Consent for information sharing

1. **Why does my blood need to be monitored if I am taking clozapine?**

   Clozapine has been associated with a serious condition that reduces white blood cell counts (agranulocytosis). Due to the risk of developing this condition, regular blood tests of white blood cell counts must take place for individuals on clozapine, to ensure that the white blood cell counts remains within the normal range.

2. **Why does my doctor need my consent?**

   The medication you are taking, clozapine, is produced by several different suppliers. Each supplier has a different monitoring system to ensure patient safety. Should your doctor and/or pharmacist (with the approval of your doctor) change the brand of clozapine you are taking, you will be transferred to a different monitored system. If this happens, it is very important that your new supplier is able to access your past white blood cell counts results in order to help your doctor ensure that you are properly monitored.

   It is also important to check with all suppliers at the start of the treatment that you have not experienced in the past a decrease of your white blood cell count with clozapine. Your consent is needed to allow this verification and sharing of information to take place.

3. **Why is personal information such as my initials, birth date, gender and health card number being collected and used for identification purposes?**

   This information will be collected and used for several reasons. Since this information is specific to you, it helps to ensure that your test results are not mixed up with those of another person on the same medication. Using this information also avoids the need to use your full name and therefore protects your privacy.

4. **Can my personal information be used for other purposes?**

   No. Your information will only be used to ensure that you are properly monitored while using any brand of clozapine.

5. **Where can I find information on the protection of health related personal information in the private sector?**

   Information on this topic can be found on the website of Industry Canada, at the following address:
   http://www.ecom.ic.gc.ca/epic/internet/inecic-ceac.nsf/en/gv00235e.html

The identification, characterization, and management of marketed health product-related adverse reactions are dependent on the active participation of health care professionals in adverse reaction reporting programmes. Any occurrences of serious and/or unexpected adverse reactions in patients receiving clozapine should be reported to Health Canada at the following address:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator 0701C
OTTAWA, Ontario K1A 0K9
Tel: (613) 957-0337 or Fax: (613) 957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866 234-2345
Fax: 866 678-6789
cadrmp@hc-sc.gc.ca

For other inquiries, please refer to contact information.

The eR Reporting Form and the eR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.

http://www.hc-sc.gc.ca/hpb-dgps/pharmac/adverse_e.html
http://www.hc-sc.gc.ca/hpb-dgps/pharmac/adr_guideline_e.html

Canada